

REMARKS

These remarks are responsive to the Office Action mailed September 15, 2009 (“Office Action”). Applicants gratefully acknowledge the Examiner’s indication that claims 35 and 40 would be allowable if rewritten in independent form. Applicants respectfully request that the rejections of the remaining claims be reconsidered and withdrawn for the following reasons.

Amendments to the claims

Claims 1, 30, and 31 are amended to recite “wherein said auxotrophic bacterial strain is non-proliferating” in the substrate. Support for this amendment is found in page 6, lines 27–28, and page 11, lines 12–14 of the specification.

Claim 12 is amended to delete the recitation of particular sequences and instead recite “an ATPase.” Support for the amendment is found, *e.g.*, in claim 14 as originally filed.

Claim 29 is amended to correct a typographical error in the recited strain accession number, as suggested by the Examiner (Office Action, page 3).

New claims 42–44 have been added. Support for new claim 42 may be found in at least page 10, lines 16-18 of the application as filed. Support for new claims 43 and 44 may be found in the application as-filed in at least claim 26 and page 5, lines 25–28.

No new matter is added by these amendments. These amendments are made solely to advance the prosecution of this application and without any disclaimer of subject matter. Applicants continue to reserve the right to pursue any cancelled subject matter in a continuing or divisional application.

Amendments to the specification

Applicants submit herewith a substitute sequence listing. The substitute sequence listing removes SEQ ID NOs: 7–11 which formed the alleged basis of a new matter rejection of claim 12. Applicants have also amended the specification to incorporate by reference the substitute sequence listing. No new matter is added by these amendments.

The substitute sequence listing is filed via EFS-Web. Applicants are not required to provide a paper copy of the sequence listing pursuant to 37 CFR 1.821(e) or the statement described in 37 CFR 1.821(f). See <http://www.uspto.gov/ebc/portal/efs/legalframework.pdf>, page 6. As required by 37 CFR 1.821(g), Applicants state that this submission does not include any new matter.

New Matter Rejection

Claim 12 has been rejected for allegedly reciting new matter, specifically, sequences of particular ATPases. The prior amendment to claim 12 simply replaced the generic recitation of "an ATPase" with particular known ATPases that were specifically identified by reference to WO 98/10089 on page 11 of the specification. Nonetheless, to advance prosecution, claim 12 is amended to delete the recitation of particular sequences and instead recite "an ATPase." The substitute sequence listing provided herewith also omits these sequences. No new matter is added by these amendments.

Novelty over Dickely

Claims 1, 9–10, 17, 24, 30–31, 44, 36–38, and 41 have been rejected as allegedly anticipated by U.S. Patent No. 5,691,185 to Dickely *et al.* ("Dickely"), specifically col. 27, lines 49–60 as evidenced by Groboillot *et al.*, *Biotechnol. Bioengineer.* 42:1157–1163 (1993) ("Groboillot") and Luksas (U.S. Patent No. 3,720,520).

Dickely expressly discloses addition of a *pur⁻* strain of *L. lactis* to milk and incubating for about 100 generations. However, Dickely is silent as to acidification of the test culture, and thus does not expressly disclose "keeping the milk under conditions where the bacterial culture is able to acidify the milk." To establish that a reference inherently discloses a claimed feature, the Patent Office must establish that the allegedly inherent feature is necessarily present in the prior art reference. See MPEP § 2112, subpart IV ("The fact that a certain result or characteristic *may* occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." (emphasis original)) (citing *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993)). As discussed in detail below, Dickely fails to inherently disclose "keeping the milk under conditions where the bacterial culture is able to acidify the milk" as

recited in claim 1, “keeping the milk under conditions where the purine or thymidine auxotrophic bacterial strain is able to ferment the milk” as recited in claim 30, or “maintaining the thus-obtained inoculated dairy flavouring and/or product for cheese flavouring starting material under such conditions that the bacterial strain of the bacterial culture is metabolically active and is able to acidify or ferment the dairy flavouring and/or a product for cheese flavouring starting material” as recited in claim 31.

The Examiner correctly acknowledges that Dickely “does not expressly teach that culturing the DN209/pFDil9 strain in milk results in acidifying or fermenting of the milk” but alleges that inoculating *pur*⁻ bacteria into milk for the purposes of testing growth would have inherently resulted in acidification or fermentation. Dickely (col. 27, lines 49–60) reports inoculation of bacterial strains into milk. One of the strains inoculated was a *pur*⁻ strain, which failed to grow. However, because the *pur*⁻ strain does not replicate in milk, acidification or fermentation can only occur if a sufficient number of bacteria are introduced (see Figure 1 of the present specification, showing that acidification decreases with inoculum). Dickely is silent as to the number of *pur*⁻ bacteria is inoculated into milk for the growth test (also correctly acknowledged by the Examiner, *see* Office Action, page 9, first full paragraph). Thus, one cannot conclude from the disclosure of Dickely that the claimed acidification or fermentation necessarily occurs.

The Examiner further cites the present specification at page 17, lines 18–19 for the proposition that the Dickely experiment would have inherently acidified milk to a pH of less than 5.5, as recited in claims 36 and 41. However, the cited portion of the specification actually contradicts Examiner’s contention. The cited statement refers the results shown in Figure 1, which shows that acidification to pH less than 5.5 was only achieved with a highest inoculums under these the test conditions. In this example, percentages referred to dilution of an outgrown culture, *i.e.*, 50% means an outgrown culture was washed and resuspended in twice its original volume. Acidification to pH less than 5.5 was only observed with the highest inoculums tested (50% and 25%) and not with 10% or 1% inoculums. In contrast, Dickely does not state what inoculum was used, and may have used an inoculum as small 0.0001% or even lower, which

would have been sufficient for a growth test but would not have achieved any detectable degree of acidification.

Finally, in the absence of express disclosure as to the number of inoculated *pur*⁻ bacteria, Dickely lacks sufficient guidance for a high level of inoculum because low levels would have been both sufficient and, indeed, desirable to practice the teachings of Dickely. In fact, low levels of inoculum would be desirable to avoid background growth due to residual purines carried over from the source culture, and to prevent the false appearance of growth due to increase in cell size without mitosis. Further, there is no question that low levels could be used in accordance with Dickely. Even a single bacterium would have been a sufficient inoculum for a growth test: over the course of 100 generations (*i.e.*, 100 population doublings) as such inoculum would have been capable of producing up to about 10³⁰ progeny. Assuming the culture becomes saturated at about 10⁹ CFU per mL (*see, e.g.*, Groboillot, pg. 1158, col. 1, final paragraph), after 100 generations the progeny of a single bacterium could saturate a culture volume of over five hundred billion Olympic-size swimming pools (2.5 million liters each). Thus, the inoculum used in the Dickely growth experiment may have been quite low (*e.g.*, 0.0001%, corresponding to an inoculum of about 1,000 bacteria per mL, or even lower), and certainly need not have been sufficient for acidification to occur. Because acidification of milk was not *necessarily* present, Dickely does not inherently disclose acidification as recited in independent claims 1, 30, and 31, or the degree of acidification recited in claims 36 and 41.

The additional cited references do not cure the failure Dickely to inherently disclose acidification. Groboillot is cited for the proposition that the generation time would be about 1 hour and that the total incubation time was thus about 100 hours. Luksas is cited for the proposition that a product for cheese flavouring starting material can encompass milk. Neither of these additional references show how the procedure of Dickely would have necessarily resulted in acidification of milk. Thus, neither Groboillot nor Luksas demonstrate that the disclosure of Dickely inherently anticipates the claims.

Non-obviousness over Dickely

The Examiner has also alleged that claims 1, 9–10, 17, 24, 30–31, 44, 36–38, and 41 were “in the alternative, . . . obvious” over Dickely. Office Action, page 6. However, no further statement is made of a proposed modification of the reference disclosure that would allegedly fall within the scope of the claimed subject matter, or any alleged reasons why such modification would have been obvious. Indeed, it is unclear whether the claims are alleged to be obvious over Dickely alone or in view of Groboillot and/or Luksas. Nonetheless, to advance prosecution, Applicants respectfully note that the claims are non-obvious over the references for at least the reasons stated above. In particular, a person of ordinary skill in the art would have been motivated to perform the process of Dickely using a low level of inoculum and thus would have avoided acidifying the milk. Moreover, none of the references disclose or suggest acidification or fermentation using a non-replicating strain, and Dickely states that the *pur*⁻ strain “cannot grow in milk not containing a purine source,” therefore the references teach away from any imaginable modification of their disclosure that would be within the scope of the present claims. Accordingly, the claims are not obvious over Dickely (alone or in combination with Groboillot and/or Luksas).

Non-obviousness over Dickely in view of Barach

Claims 11, 34, and 39 have been rejected as allegedly obvious over Dickely in view of Barach *et al.* U.S. Patent 4,294,930 (“Barach”). Barach is alleged to teach that “when culturing a microbe in milk, it is desirable to use 10^8 CFU/mL.” However, Barach fails to cure the deficiencies of Dickely, including the failure to disclose or suggest acidification of milk by a non-replicating strain (discussed in detail in the preceding section). Moreover, the proposed combination of Barach and Dickely is inconsistent with the reference disclosure, as Dickely at most teaches that a *pur*⁻ strain of *L. lactis* is unsuitable for milk fermentation due to its inability to grow in the substrate. Whatever inoculum is taught by the secondary reference is immaterial because the secondary reference only concerns fermentation resulting from inoculation of a replicating strain. Accordingly, it would appear that the references do not provide (nor has the Examiner identified) any valid motivation to inoculate 10^8 CFU/mL of a non-replicating *pur*⁻ strain into milk, and moreover the references do not provide any reasonable expectation that

sufficient acidification would be obtained thereby. Accordingly, reconsideration and withdrawal of the rejection is respectfully solicited.

Non-obviousness over Dickely in view of Nilsson

Claim 28 has been rejected as allegedly obvious over Dickely in view of Nilsson *et al. Mol. Gen. Genet.* 235:359-364 (1992) ("Nilsson"). Nilsson is alleged to teach strain DN105, recited in claim 28. However, Nilsson fails to cure the deficiencies of Dickely, including the failure to disclose or suggest acidification of milk by a non-replicating strain (discussed in detail above). Whatever *pur*⁻ strain is taught by the secondary reference is immaterial because neither the primary nor the secondary reference discloses or suggest acidification of milk by a non-replicating *pur*⁻ strain. Accordingly, reconsideration and withdrawal of the rejection is respectfully solicited.

CONCLUSION

Applicants submit that this amendment addresses all of the issues raised in prior Office Actions and places all claim in condition for allowance. An early notice to that effect is respectfully solicited. The Examiner is invited to contact the undersigned directly at (202) 419-2021 if it would be helpful for resolution of any remaining issues.

It is respectfully submitted that no fee is required for entry of this amendment and consideration of this application. However, in the event any fees are deemed necessary, the Commissioner is authorized to charge such fees to the undersigned's Deposit Account No. **50-0206**.

Respectfully submitted,
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